T-computers and the Origins of Time in the Brain

Scott M. Hitchcock[1,2]

Abstract

Recent research has *identified the components* of the brain that appear to time label information from observed sensory events, store the labeled information in memory and then using the time labels for two or more events to compute their time differences, time intervals, elapsed times or 'lifetimes'. Time differences are the basis of the 'time' numbers we read from clocks and compute in our brains. Time is our map of change. Maps are abstractions of information and can be used to construct useful devices such as space-time. A general time computer or T-computer model is outlined that shows how observed signals can be processed into time labeled information states infostates by our instruments or our brains. The observer can communicate the 'time' computed for observed events using consciousness and language signals to drive sound signals in the vocal cords for instance. The ‘problem of time’ is near a realistic solution now that the brain's T-computer has been identified. The brain is the 'local' creator of time, space, and space-time as our special maps of the reality we 'observe' and participate in.

Key Words: T-Computers, Information

NeuroQuantology 2003; 4: 393-403

[1] Other papers by Scott M. Hitchcock are at http://www.msu.edu/~hitchco4/. Correspondence hitchco4@pilot.msu.edu.

[2] This version of the paper was slightly revised on January 5, 2003, by the deletion of the J. Barbour reference. It was replaced with J. B. Priestley’s 1964 book “***Man and Time***” which I only found just recently. This book pre-dates Barbour’s ideas about *change as the source of time* and I felt that I should refer to the earlier source for historical correctness. There may be even earlier references that I have not yet found. I have said in my earlier papers “No change means no time”. I arrived at this while completely unaware of both Priestley’s work in 1964 and Barbour’s 1999 book “The End of Time” and his web page. If some of my other ideas are inadvertent reinventions of other people’s work, I would appreciate references from the reader. Please look at the extensive references in my earlier papers before contacting me since many other people’s papers are *implicitly referred to* via the references to my own earlier papers I use in this paper.

"Why is the flow of psychological time identical with the direction of increasing entropy? The answer is simple: Man is part of nature, and his memory is a registering instrument subject to the laws of information theory. The increase of information defines the direction of subjective time. Yesterday's experiences are registered in our memory, those of tomorrow are not, and they cannot be registered before tomorrow has become today. The time of our experience is the time which manifests itself through a registering instrument. It is not a human prerogative to define a flow of time; every registering instrument does the same. What we call the time direction, the direction of becoming, is a relation between a registering instrument and its environment; and the statistical isotropy of the universe guarantees that this relation is the same for all such instruments, including human memory."

Hans Reichenbach

INTRODUCTION

What is Time? *Time* is a form of information (a 'label', 'number', or 'dimension', etc.) we have invented to *quantify* and *measure* (usually a 'number') *changes* in the things that fill the world around us as well as the life processes within us. The time labeled information state is a new state of mind that is a sum of observed sensory information combined with a time label. One can think of this as a 'word' of '**a**' bits of observed information combined with '**b**' bits of time labeling information forming a 'word' or infostate, **I**, at a time, **t**, of $\mathbf{a + b = I_t}$ total bits that can be 'perceived' and compared with other time labeled infostates as well as 'stored' in accessible sequential memory locations. This infostate is only one of many in a sequence that characterize evolving configuration changes of the observed phenomena around us. Time *is* a construction of our brains used to organize sequential patterns of detected information from our senses. *How* we create time is the key to understanding the way we use time to create *maps* of change and build scientific models of the universe. We are now capable of examining our use of 'time' as a dimension. The brains' builds maps of changing patterns in order to extrapolate how these patterns might evolve. These maps of reality are formalized into physical 'laws' using mathematical structures such as space-time. 'Time' is the result of our brain's need to detect patterns of change for our own survival. Time is but also for understanding the beauty of all life and inanimate things as they change and evolve through a process of creating new forms and structures. Time mapping processes in our brains are traceable back to the DNA that builds our bodies and runs the biological clocks of life.

Time is a form of information that represents a measure of change. The real 'problem of time' is about how we compute 'time' and build time and space maps using our instruments and our brains.

Let us look at Time as a form of *information* Hitchcock 2002, Hitchcock 2001, Hitchcock 2000, Hitchcock 1999) that *represents measures* of *change*. J. B. Priestley said

"*No change, then, no Time***"** (Priestley 1964) This means that 'change' is a necessary condition for the ***creation*** and ***computation*** of time as well as the use of time as a 'dimension'. 'Change' in the shape, contents, energies, and other physical and chemical properties of substances (matter) forming systems spread throughout the universe is observed as signals originating in, or modified by, the reconfigurations of these islands of matter. We exist as active evolving complex systems of matter on the sea of the vacuum. The distribution of is used to construct a map of the vacuum that we call 'space'. 'Forces' such as the strong, electromagnetic, weak, and gravitational interactions drive the reconfigurations. The real 'problem of time' is about how we compute 'time' and build time and space maps using our instruments and our brains.

The recent work of Rao, Mayer, and Harrington (Rao 2001) has isolated the physical components of the T-computer in the Brain; "Early cortical activation associated with encoding of time intervals was observed in the right inferior parietal cortex and bilateral premotor cortex, implicating these systems in attention and temporary maintenance of intervals. Late activation in the right dorsolateral prefrontal cortex emerged during comparison of time intervals."

Exactly how information is processed into 'time' by these components at the quantum level is still an open question. The components they have identified are at this point still 'black boxes' that take an input and generate an output. The deeper cellular and sub-cellular computational and information processing activities are as yet to be identified. The identification and functional properties of these components is still important since they act as computational systems that are identified in the T-computer model. The relationship of these brain areas to the parts of a T-computer will be discussed later in this paper. We will also look at the role of the T-computer and consciousness. First we want to describe the T-computer model and outline how time labels events, calculates time intervals, differences, and 'lifetimes'. Once 'times' are identified with events we have the basis for creating time as a dimension used in maps like space-time and how 'arrows of time' are created and identified with the evolutionary processes of the things that make up our universe.

T-COMPUTERS AND TIME CREATION

T-computers (Hitchcock 2002, Hitchcock 2001, Hitchcock 2000, Hitchcock 1999) are essential to our maps of reality. They are used to create ordered sets of time labeled ***observed*** events or time calibrated internal thought processes whose 'linear' or non-linear causal time ordering may be the location of the infostates representing the events in memory and their contents. An ***infostate*** of a system is the set of configuration observables for that system along with the ***information content*** usually expressed as the wavefunction for the system. Information originates in quantum system and is processed as quantum or classical states of the neural networks of our brains. This is one of the places where the 'neural' ***merges*** with the 'quanta' of 'change'.

Time is a form of information computed by a T-computer (see Fig. 1). Signals created during a configuration change in a system, can carry information to the detectors of the observer. The detectors convert the signal into another signal that can be sent to the T-computer and other information processing networks. The signals deposit information in each ode or logic gate of the network by the creation of a reconfiguration infostate there. The gate can then act on the infostate to produce anew one to send along the network or store it as a memory of the event information brought to the observer by the original signal. The T-computer time labels the infostate in the first stage, then stored then in a working memory. The working memory can be addressed by the T-computers second stage, which can *retrieve* or *copy* infostates from memory for two events and compare (subtract) their time labels in order to calculate elapsed 'time' between the events. The stored infostates can be the 'start' and 'stop' signals for a single event or the time labels for two different events. In either case it is the 'time difference' that is the output of the T-computer. This is the *time* we normally associate with the coordinates of a conventional event located by one dimension of time and three of space in space-time diagrams.

T-computers used to create ordered sets of time labeled *observed* events or time calibrated internal thought processes whose 'linear' or non-linear causal time ordering may be the location of the infostates representing the events in memory and their contents.

Let's examine how *time-independent* information flow (sequential 'changes' of states of network components) through a T-computer starting with signal detection from 'observed' events processed in *parallel* with coincident 'clock' signals moves is an serial path to the T-computers 'time' computer ending with a 'time' output. This 'time' number can now be processed into the 'time' of space-time.

STANDARD SIGNALS FROM 'CLOCKS'

In order to create time we begin by pairing a signal representing a reference event acting as a standard and a signal from the observed event representing the information we want to 'time label'. Since the general idea of a clock is something that already 'measures' time, for the purposes of this paper we will *define a* ***clock*** *as any system that produces signals that can be used to compute time by a process of signal mapping of the clock signal to another signal that is to be 'time labeled' by a T-computer*. In this way we can think of a clock as a system that 'changes' in such a way as to produce signals without any explicit or implicit *measurement* of 'time'.

Next we address the nature of a clock as a standard signal producing system that emits calibration signals in a repeating, regular, and precise way. The atomic clock is a system in which the repeating of signals is driven by classical electronics operating on a quantum system. Energy is provided in order to reset the quantum system after it has

decayed in a time-independent 'lifetime' as a function of the systems composition and stability. This controls the system in a repeatable way.

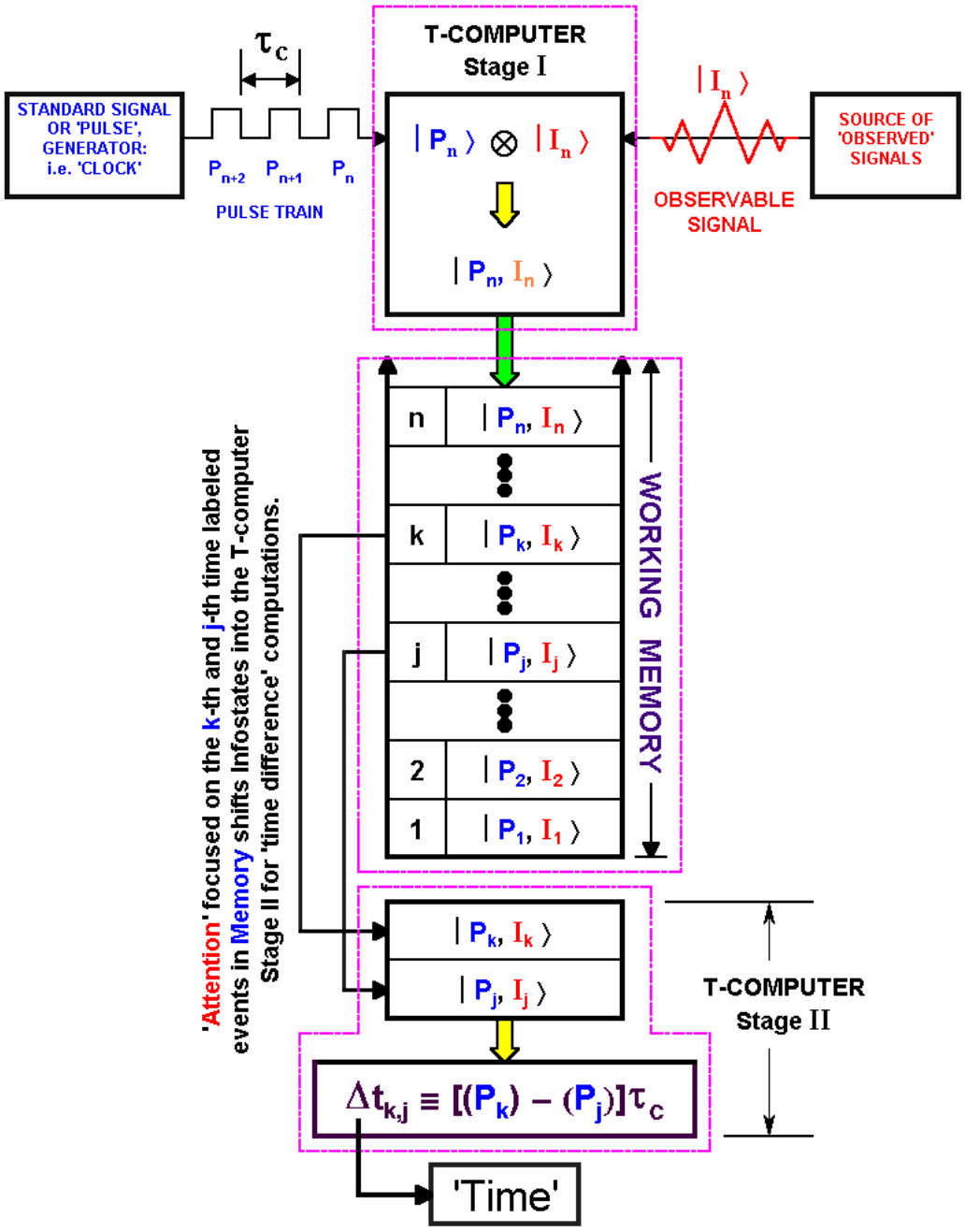

Figure 1. The T-computer.

The 'dimensions' of the *units* of 'time' we give to the 'lifetime' of a state come from ***Planck's constant, ħ,*** which acts a dimensional conversion factor transforming the time-independent changes and information in the quantum systems reconfiguration process on the right hand of the equation below to the 'time' on the left.

$$\tau = \hbar / \Gamma$$

We will define a ***clock*** as any system that produces signals that can be used to compute time by a process of signal mapping of the clock signal to another signal that is to be 'time labeled' by a T-computer

On the right we have the '*decay rate*' Γ (Veltman 1995)**.** It curiously does not have 'units' of time but rather *energy*. Energy changes involved in the decay process are controlled by the fundamental forces between the particles that make up the quantum system an their geometric instability. This causes the system to decay in a finite lifetime as compared with another system that decays in a 'standard' lifetime such as the atoms in an atomic clock. The dimension of 'time' on the left comes from Planck's constant which encodes the relationship between two quantum systems that provides the information used to define time as a 'relational' concept relative to at least two changing systems. This is discussed in more detail in (Hitchcock 2001, Hitchcock 2000, Hitchcock 1999).

While one may say that the units of energy when reduced to fundamental observables has 'time' in it, one can measure the energies involved in the reconfiguration changes as numbers such as positions of line spectra on a detector array without considering time. If one had no concept of time one could still measure the energies of different wavelengths of light!

In figure 1 the standard signal generator on the upper left could be an 'atomic clock' or other 'clock' device that creates signals in a regular way that when paired with observed signals can be used to define time as 'time label differences'.

SIGNALS FROM 'OBSERVED' SYSTEMS

All unstable systems in the universe produce information when they undergo a 'change' to a more stable configuration. At the quantum level we see this in the emission of light when electrons jump to lower energy configurations. The light emitted by these atoms are signal that carry information about the quantum structure of the electronic orbitals. Spectroscopy gave us the information to build the quantum model of these systems by providing information that was carried identically with the photons. Signals can be the result of reconfiguration in many body systems acting collectively. The changes in the collective excitations of these systems can result in photons, phonons, excitons, and many other 'quantum' signals. They can also give rise to mesoscopic and macroscopic signals such as electromagnetic 'waves' and sound waves in the limit of many quantum signals acting collectively as a 'classical' object.

The signals may also be chemical transmitters such as those involved in biological

detection and information processing systems. Complex causal networks can be composed of hierarchical *plateaus of complexity* or *POCs* from atoms to molecules to macromolecules to organelles and cell nuclei to cell membranes, to cells and groups of cells acting collectively as organs and organs acting collectively to form organisms. At each level, 'changes' in configurations can produce information and signals represented by, **[I_n** ñ, that can be time labeled by a standard clock by paring it with a *countable* clock pulse, **[P_n** ñ in figure 1. This is the information detected by our senses and their extensions in the form of instruments.

T-COMPUTER STAGE I COMPUTATIONS

This is where 'time labeling' of detected information begins. Modeling this process is now possible due to the development of quantum information processing methodology (Nielsen 2000) that allows us to identify physical information flow in causal networks using quantum computation.

The incoming signal from the standard clock and the target signal (i.e. the observed signal from the source) are detected and converted into a configuration of the detectors called an *infostate* containing the information deposited in the detectors that represents some or all of the observables involved in the creations of their respective signals and sources. Infostates can be acted on by the subsequent logic of the nodes or gates in the causal network forming the time computer in much the same way that CCD camera images of objects can be 'time labeled' and uploaded into a computer for image processing.

The two signals can be thought of a quantum or classical words whose individual entries are quantum or classical bits as in quantum or conventional computers. If each word representing the clock and observed signals and their information content is put together to form a composite quantum or classical word, then this *concatenation* process is identified with the 'direct tensor product', Ä, as opposed to summation +. This is because the new state formed by the two infostates is the collective excitation state of a 'composite' many-body quantum system *not* the linear superposition of states identified with the wavefunction for a single isolated system such as that of a hydrogen atom. The composite infostate is one with both infostates *concatenated* together into a larger infostate by the T-computer Stage I detectors and associated processing logic. The new infostate is:

$$\mathbf{[P_n, I_n\tilde{n} = [P_n\ \tilde{n}\ \ddot{A}\ [I_n\ \tilde{n}}$$

At this point $\mathbf{P_n}$ is the n^{th} pulse number as counted by the T-computer in the detection sampling 'window' closest to the n^{th} observed signal infostate detection 'event' where the information content of this signal is $\mathbf{I_n}$. The observed information now has a '***pre-time label'***, $\mathbf{P_n}$, whose conversion into conventional *event times* used in space-time maps will be done in the T-computer Stage II.

In the case of the brain, the detectors may be essentially separate from the

T-computer Stages I. The detectors, such as eyes, send the information extracted by a signal conversion event (sometimes erroneously referred to as the *collapse* of the photon wavefunction when in fact the photon is converted to a retinal infostate by the processing of it into a collective excitation emitted as a nerve impulse) via the *optic pathway* to the *T-computer Stage I* in the brain.

WORKING MEMORY

This is the physical system, accessible, that stores the '*pre-time labeled'* infostates generated in the T-computer Stage I. It is accessible by the *attention* mechanism that selects given infostates for further information processing by the T-computer Stage II leading to the *time difference* computations needed for the construction of 'time' as a *dimension* with *direction*.

T-COMPUTER STAGE II COMPUTATIONS

The *attention* of the observer identifies and grabs the infostates for two events from the working memory in order to find a *time difference* between their *pre-time labels*. It loads them into a 'comparator' to compute the difference between the *pre-time labels* for the two infostates in order to compute D**t** = *'conventional time'*. A *pre-calculation* can also occur in which the two events are first compared to some defined **t = 0** or $\mathbf{t_0}$ reference event infostate allowing the assignment of a conventional time label to each event in working memory whose meaning is the elapsed time with respect to a standard event. The time difference between the two events is the difference between the newly assigned final *time labels*. The time difference can also be computed directly without the $\mathbf{t_0}$ reference event!

Either way the pre-time labeled events can be computed into conventional time labeled events with a 'time' number associated with each. These time numbers are what we usually call the event time but they have to be computed first by a signal mapping and labeling process in the T-computer before they can surface in consciousness as *the time something happened*.

Once conventional time labels have been attached to an infostate representing an observation, then they can be stored in a *'Long Term'* or '*Permanent'* memory as an ordered set of time labeled events. This set can be mapped onto the real number line for the creation of a 'timeline' or time axis in the case of space-time.

T-COMPUTERS IN THE BRAIN

T-computers detect signals and process them as infostates propagating sequentially (in space not necessarily 'in time') through the physical logic gates forming a causal network. The prime function of the T-computer is to pair the information representing an observed event with a 'time label'.

Based on the evidence for 'temporal processing' in the brain (Rao 2001), there are biological T-computer components that function in the same way as the idealized T-computer model described above. The brain receives information from the senses. In order to identify its causal relationship to other events it needs to time label this information and store it in a working memory.

The brain receives information from the senses. In order to identify its causal relationship to other events it needs to time label this information and store it in a working memory

Recent fMRI evidence (Rao 2001) implicates the *right inferior parietal cortex* and *bilateral premotor cortex* in the mechanism of '*attention*' as well as the initial organization and storage of time labeled infostates in a '*working memory*' acting as the *T-computer Stage I* in the brain. The T-computer Stage II is seen in temporal processing activities in the *right dorsolateral prefrontal cortex* where the comparison of the two time intervals takes place. The time labeled infostates created in Stage I, including placement of time labeled infostates in memory, are accessed and compared in Stage II in order to determine which of two sequential intervals was 'longer' and therefore determining a 'time output' in the form of a 'response' by the subjects.

This may be the site in the brain where the common conception of the 'time' (as a 'time difference') for an event or between events originates and in some sense where time first emerges in consciousness as an abstract measure perceived 'change'. From here the brain can construct maps using the time associated with onset of events, lifetimes of events, or time intervals between events as a dimension or axis like that used in space-time. The details of this process are still under investigation and outside the scope of this paper. 'Time' differences and the information defining the order of infostates representing the observed events can be used to create temporal pointers or 'arrows of time' between 'earlier' and 'later' infostates. This is one of the possible 'outputs' of the T-computer working with consciousness to create time.

WHAT 'TIME' IS IT?

To answer this question one must engage the T-computer and other information processing and signal generating devices such as the vocal cords needed to 'say' the time. The computation of the difference between the time labels for any two infostates results in another 'bit' of information that we call the 'time' elapsed between the two observed events. From this perspective, 'time' does not exist a priori, but is in fact a computed measure of change. The construction of a 'direction' and 'dimension' for 'arrows of time' follows from the ordered sets of numbers or label states added to observed 'infostates' originating in unstable systems. Time is what we compute it to be using our T-computers and the time part of our space-time maps. The time we give is always referenced to some standard system whose periodic changes produce reference information by which we can

say *what the time is*.

Recognition that 'time' is created by complex systems capable of 'computing' it, may clear up 'time' related paradoxes and issues related to causality, information theory, and the 'experience' of time inside complex states of 'consciousness'.

SUMMARY

In this brief paper I have attempted to outline a new way of thinking about time. I would like to summarize by stating the following three conclusions.

1. 'Change' creates signals that carry information to other systems in space.
2. Detection of signals provides information that a T-computer can compute into time labeled infostates representing observed phenomena or events.
3. Our brain's T-computer computes 'time' and 'time differences' for events. The computed times for events can be used to build maps of change such as 'space-time'.

In the brain the T-computer 'time labeling' components are found in the right inferior parietal cortex and bilateral premotor cortex. The T-computer the computes a 'time differences', D**t,** and therefore the 'time', '**t**' (for D**t = t-t$_0$**, where **t$_0$=0**) tagged to an event.

This time can be interpreted as elapsed time between events or the lifetime of a reconfiguration process. The *ordered set of these time numbers* can be used to construct a timeline. The 'order' for these sets follows from the order of integer or real numbers following from the generator function defined by the Peano axioms of mathematics. Timelines are the basis for the time axis used in space-time. The dimension of time is the dimension of the time label, if we use a real or integer number then *dimension*=1. The direction of time is the direction of the increasing time labels.

Time is a construction of the brains signal mapping, time labeling, event storage and retrieval in memories and the T-computers ability to calculate the 'time' differences which become the 'time' (with an implicit or defined initial time of **t = 0** for instance) component of space-time maps. The brain also constructs the *dimensions* and *directions* associated with the *space components* of *space-time*.

We project the laws of physics onto our maps as a result of our computing the relationships of causal and effect for events on our maps. Using the patterns we encode as the laws of physics, we can estimate how things change and guess how emerging configurations of matter evolve.

Many questions remain about how our brains create time from the molecular scale upward to 'consciousness' but the pioneering work of Stephen M. Rao, Andrew Mayer, and Deborah L. Harrington has opened the door to understanding the connection between the changes in an evolving universe and the time we create with our brains to measure it. The ideas I have presented here indicate that a correct conception of 'time' requires that

we understand 'time as information' and that time is as *real* as *information* is[3].

ACKNOWLEDGEMENTS

I would like to thank Sultan Tarlaci for his persistence to write this paper. I thank Vladimir A. Petrov for 'discovering' my work, continued moral support and sharing his considerable wisdom with me over the last 3 years. I also thank my wife Toni, and the rest of my family and friends for their patience. All are blameless for my errors. *Ad Astra, Ab Intra…*

REFERENCES

1. Stephen M. Rao, Andrew Mayer, and Deborah L. Harrington, The evolution of brain activation during temporal processing. *Nature Neuroscience*, 2001; 4:317-323.

2. Hans Reichenbach. The Direction of Time. Edited by Maria Reichenbach, Dover Publications, Inc., Mineola, NY, 1999.

3. Scott M. Hitchcock. The Creation of Time from Substance and Space. Accepted June 2002 for publication in the Space-time and Substance International Physical Journal at http://spacetime.narod.ru/

4. Scott M. Hitchcock. Time and Information: From Feynman Diagrams to Feynman Clocks and Beyond. 2001. Available at LANL http://xxx.lanl.gov/abs/quant-ph/0111025.

5. Scott M. Hitchcock. Feynman Clocks, Casual Networks, and Hierarchical Arrows of Time in Complex Systems From the Big Bang to the Brain. 2000. Available at http://xxx.lanl.gov/abs/quant-ph/0010014

6. Scott M. Hitchcock. Quantum Clocks and the Origin of Time in Complex Systems. 1999. Los Alamos National Lab, LANL e-Print Archives http://xxx.lanl.gov/abs/gr-qc/9902046.

7. J. B. Priestley. Man and Time. Crescent Books, London, UK, 1964. Page 64 "*No change, then, no Time*".

8. Martinus Veltman. Diagrammatica: the Path to Feynman Diagrams. Cambridge University Press, UK, 1995. See Appendix D, pages 243-244.

9. Michael A. Nielsen and Issac L. Chuang. Quantum Computation and Quantum Information. Cambridge University Press, UK, 2000.

[3] "I could be wrong, I could be right…may the road rise with you…" from the song 'Rise' by P.I.L.

The evolution of brain activation during temporal processing

Stephen M. Rao[1,4], Andrew R. Mayer[1] and Deborah L. Harrington[1,2,3,4]

[1] *Department of Neurology, Medical College of Wisconsin, Milwaukee, Wisconsin 53226, USA*

[2] *Department of Veterans Affairs, Albuquerque, New Mexico 87108, USA*

[3] *Department of Neurology, University of New Mexico, Albuquerque, New Mexico 87113, USA*

[4] *These authors contributed equally to this work*

Correspondence should be addressed to D.L.H. (dharring@unm.edu)

Timing is crucial to many aspects of human performance. To better understand its neural underpinnings, we used event-related fMRI to examine the time course of activation associated with different components of a time perception task. We distinguished systems associated with encoding time intervals from those related to comparing intervals and implementing a response. Activation in the basal ganglia occurred early, and was uniquely associated with encoding time intervals, whereas cerebellar activation unfolded late, suggesting an involvement in processes other than explicit timing. Early cortical activation associated with encoding of time intervals was observed in the right inferior parietal cortex and bilateral premotor cortex, implicating these systems in attention and temporary maintenance of intervals. Late activation in the right dorsolateral prefrontal cortex emerged during comparison of time intervals. Our results illustrate a dynamic network of cortical-subcortical activation associated with different components of temporal information processing.

Humans are remarkably proficient at perceiving the passage of time and producing precisely timed behaviors, many of which depend upon explicit prospective temporal judgments. For these events, multiple processes seem to determine our subjective perception of current time for intervals lasting several hundreds of milliseconds to several seconds. Most theories of prospective timing embody similar components[1], including an internal timekeeper, attention and memory[2,3]. A clock metaphor is used to describe the timekeeper mechanism, which represents subjective time through the accumulation or readout of pulses, possibly generated by oscillators. Our perception of time, however, is intimately related to the level of attention given to the passage of time. When attention is diverted, a systematic shortening of subjective duration occurs, implying that pulses from the timekeeper may be lost[4]. Attention may also mediate the flexible starting and stopping of pulses from the timekeeper, which enables anticipation of predictable events[5]. Hence, a representation of subjective time emerges from the interplay between timekeeping and attention mechanisms. This representation is then passed on to working memory, a short-term repository where interval representations are maintained and manipulated in accord with current goals (for example, comparing two intervals of time)[6]. Working memory functions can therefore alter stored representations of time as well. The combination of these different component processes gives rise to the subjective perception of time, although the relative contribution of each might differ depending on the interval duration or the cognitive demands of timing events[7].

The neural systems that support different component processes of time perception are a matter of debate. The basal ganglia and lateral cerebellum have been logical candidates for hypothetical timekeeping operations, as damage to these brain regions commonly disrupts behaviors that depend upon precise timing, such as rhythmic movements in Parkinson's disease[8] and regulation of agonist–antagonist muscle activity (for example, dysmetria) in cerebellar damage[9]. Although these movement abnormalities could be attributed to disruption of more generalized motor execution functions, the basal ganglia and cerebellum do seem to mediate time perception. Studies of Parkinson's disease patients[10,11] and pharmacological investigations in animals[12,13] have argued that timekeeping operations are regulated through dopamine neurotransmission in the striatum. Human lesion studies indicate that the lateral cerebellar hemisphere and its primary output, the dentate nucleus[14–18], are also involved in timekeeping mechanisms. Nonetheless, it has been difficult to isolate timekeeping and attention operations from working-memory and response implementation processes[1]. Timing deficits after basal ganglia or cerebellar damage could also be due to abnormalities in interconnecting cortical systems commonly associated with some or all of these processes[19,20]. Fewer studies have examined the involvement of the cerebral cortex in time perception. Focal lesion investigations in animals and humans have shown that the frontal and parietal lobes are also essential for accurate time perception, perhaps due to their purported attention and working memory functions[14,21,22]. Others have posited a role for the supplementary motor area[23], but this has been difficult to assess because focal lesions are uncommon in this region.

Functional imaging techniques can be used to dissect the contribution of each component of multiple neural systems, although studies of timing using these methods have produced conflicting or ambiguous results to date[7]. Most research[24–27] has focused on motor timing, making it difficult to separate activa-

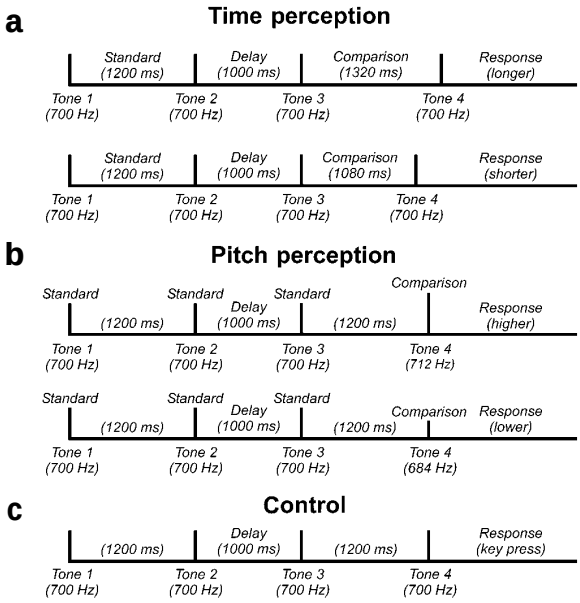

Fig. 1. Trial events in the time perception (**a**), pitch perception (**b**), and control (**c**) conditions. In the time perception condition, subjects indicated whether the comparison interval (defined by tones 3 and 4) was longer or shorter than the standard interval (defined by tones 1 and 2). In the pitch perception condition, subjects indicated whether the comparison tone (tone 4) was higher or lower in pitch than the standard tones (tones 1, 2 and 3). In the control condition, subjects pressed a key after the presentation of the four tones.

tion in systems traditionally associated with motor control, such as the basal ganglia and cerebellum, from those supporting timekeeping or other cognitive processes. Two PET studies[28,29] have specifically examined time perception. Unfortunately, the time scale of PET scanning is limited to blocked-trial designs that cannot disentangle processing associated with encoding an interval from processing associated with decision making and implementing a response. We reasoned that fundamental insights into this issue could be gained by studying the time course of brain activation patterns associated with different components of a time perception task. The present study exploited the finer temporal resolution of event-related functional magnetic resonance imaging (fMRI) to isolate patterns of brain activation that correlated with encoding time intervals from those associated with comparing two time intervals and implementing a response. Timing theory suggests that activation in systems integrally involved in encoding or formulating a representation of time (pacemaker and attention operations) should develop at the onset of a to-be-timed event[2,3], followed by activation in systems concerned with manipulating information in working memory (comparing intervals) and implementing a response.

We obtained fMRI scans of seventeen subjects as they performed three different tasks, the order of which was counterbalanced across subjects. In the time (T) discrimination condition, two tones (50 ms) separated by 1200 ms (standard tone-pair) were presented, followed by a 1-s delay and then a comparison tone-pair (Fig. 1a). Subjects indicated whether the comparison tone-pair was longer or shorter than the standard. To better separate neural systems specific to timing, subjects also performed a pitch (P) discrimination condition in which the auditory events were similar except that subjects indicated whether the fourth tone was higher or lower in pitch than the first three tones (Fig. 1b). Neural systems involved with processing time and pitch information were identified by contrasting imaging runs in each discrimination condition with a sensorimotor control (C) condition in which subjects responded after the presentation of two isochronous tone pairs of identical pitch (Fig. 1c). The T and P conditions were then contrasted to specify systems unique to time discriminations. These subtractions were conducted at each of four scanning intervals after trial onset (2.5, 5.0, 7.5 and 10.0 s). In all conditions, the typical motor response occurred approximately 4.5 s after trial onset (Fig. 2). Allowing 5 s for the hemodynamic response to peak, we proposed that the 2.5- and 5.0-s intervals after trial onset should reveal brain activation patterns specific to encoding time intervals. In contrast, the 10.0-s scanning interval should include activations associated with contrasting the standard and comparison intervals and implementing the response. Overlap between these processes should be particularly evident during the 7.5-s scan, due to encoding of the comparison interval. The results reported here show early sustained activation of the basal ganglia and right inferior parietal cortex, implicating these systems in formulating representations of time. Though activation in the cerebellum was more robust during time than pitch discriminations, activation was located in the vermis and unfolded late, suggesting a more general involvement in cognitive or sensorimotor functions. The evolution of activation in the bilateral premotor and right DLPF cortex differed from each other, consistent with previous work implicating these systems in different aspects of working memory.

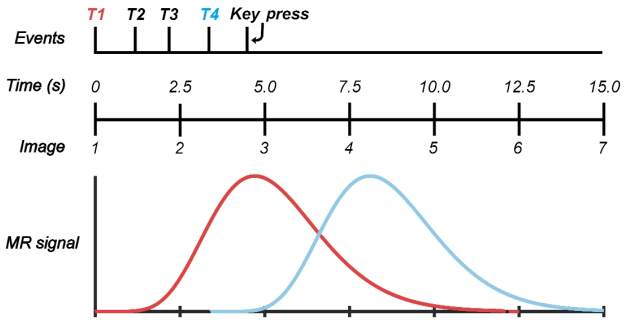

Fig. 2. Temporal relationship among the trial events, acquisition of images and hypothetical hemodynamic response functions to different task components. Seven scans were acquired during each 17.5-s trial (a 2.5-s interval between the seventh image and the first image of the next trial is not illustrated on the timeline). The first scan was acquired at the onset of the first tone (T1). The fourth tone (T4) was presented an average of 3.4 s after trial onset. The typical key press response occurred 4.5 s after trial onset. The two hypothetical time course functions illustrate early versus late MR signal responses to different trial events. An early response corresponding with the encoding of temporal information (red plot) would have a maximal signal change at 2.5 and 5.0 s after trial onset. In contrast, a late response due to decision making and response preparation processes (blue plot) would be observed primarily at 7.5 and 10.0 s after trial onset.

RESULTS

Behavioral data collected during scanning showed that response times and accuracy correlated with the difficulty of time and pitch discriminations. Reaction time was typically longer (Fig. 3a, $F_{5,76} = 4.2$, $p < 0.01$; Fig. 3c, $F_{6,87} = 4.0$, $p < 0.01$) and accuracy poorer (Fig. 3b, $F_{4,57} = 8.1$, $p < 0.001$; Fig. 3d, $F_{7,112} = 2.7$, $p < 0.025$) when the comparison stimuli were closer in time or in pitch to the standard stimulus. There were no significant differences between the two discrimination conditions in overall accuracy (T, 83 ± 3%; P, 78 ± 3%) or reaction time (T, 1111 ± 76 ms; P, 1076 ± 54 ms). Reaction times for the C condition (707 ± 39 ms) were significantly faster ($F_{1,16} = 48.9$, $p < 0.0001$) than those for the time and pitch conditions.

During the early imaging epochs (2.5 and 5.0 s), which emphasize encoding of temporal information, subcortical activations specific to the T condition (Table 1) were observed within the right putamen, head of the caudate nucleus bilaterally, and right centromedian and ventroanterior thalamic nuclei (Fig. 4a). Early activation specific to the T condition was also observed in various cortical regions (Fig. 5): right intraparietal sulcus (BA 40), bilateral dorsal and left ventral premotor areas (BA 6), and bilateral lateral temporal cortex (BA 21/22). Activation specific to the T condition was sustained during the 7.5- and/or 10.0-s imaging epochs in most of these regions. In the P condition, areas of activation during the early imaging epochs overlapped with those in the T condition. In both the T and P conditions (Table 2), activity unfolded early within the medial wall (preSMA and SMA proper, BA 6, and anterior cingulate, BA 32; Fig. 4c) and the anterior insula/frontal operculum (Fig. 4a), but was sustained during later epochs as well.

During the later imaging epochs (7.5 and 10.0 s), which included decision and response selection components of the tasks, activation specific to the T condition (Table 1) was observed in the posterior vermis (tuber) of lobule VIIB of the cerebellum (Fig. 4b) and the right dorsolateral prefrontal (DLPF) cortex (BA 46/10/9; Fig. 5). All other activation foci were observed in the left hemisphere in both the

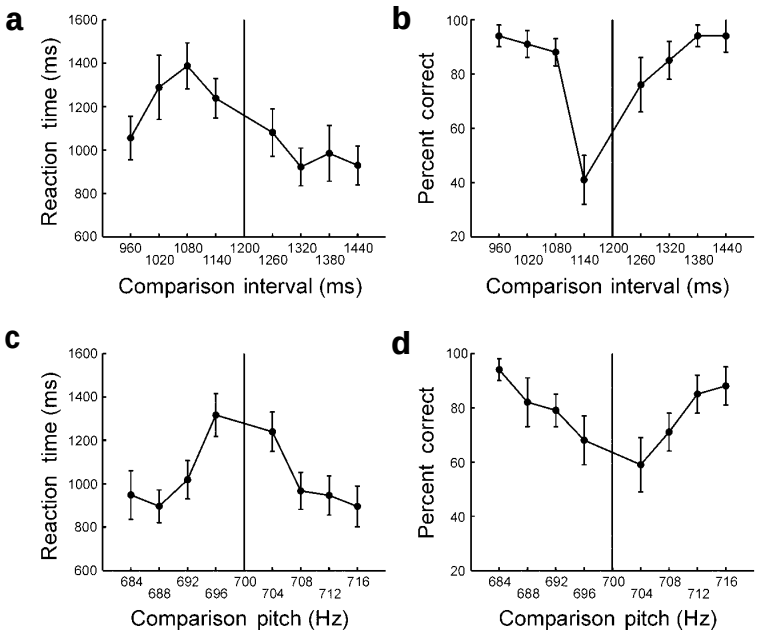

Fig. 3. Mean (± standard error of mean) reaction time and percent correct for the time perception (**a**, **b**) and the pitch perception (**c**, **d**) conditions. Data are depicted as a function of the comparison interval or comparison pitch.

Table 1. Stereotaxic brain atlas coordinates[49] for Time > Control subtraction.

Location (Brodmann Area)	Hemisphere	2.5	5.0	7.5	10.0
Basal Ganglia					
Medial caudate (head)	R		12, 7, 3	12, 6, 4	
	L		–12, 7, 5	–9, 7, 2	–8, 4, 8
Lateral caudate (body)	R				15, 6, 19
Putamen	R	22, 8, –1			23, 6, 8
					26, 6, –2
	L				–20, –1, 5
Cerebellum					
Vermis (tuber, lobule VIIB)	B			–3, –70, –30	2, –70, –29
Thalamus					
Centromedian nucleus	R		4, –21, 0	4, –21, 0	
Ventroanterior nucleus	R		4, –11, 0	5, –10, 0	
Frontal					
Dorsal premotor (6)	R		23, –7, 48	23, –3, 52	46, 1, 49
	L		–45, –7, 47		
Ventral premotor (6)	R		46, 8, 24		
	L	–54, –13, 26	–51, –15, 27		
Dorsolateral (46/10/9)	R			34, 23, 25	31, 46, 22
					41, 29, 22
Parietal					
Intraparietal sulcus, Angular gyrus (40)	R	38, –40, 41	36, –43, 40	37, –47, 38	30, –56, 35
Superior parietal lobule, Precuneus (7)	R				10, –68, 44
Temporal					
Superior temporal (22)	R		51, –39, 6		
Middle temporal (21)	L		–46, –56, 4		

R, right; L, left; B, bilateral. The activations reported in this table were not observed in the Pitch > Control subtraction.

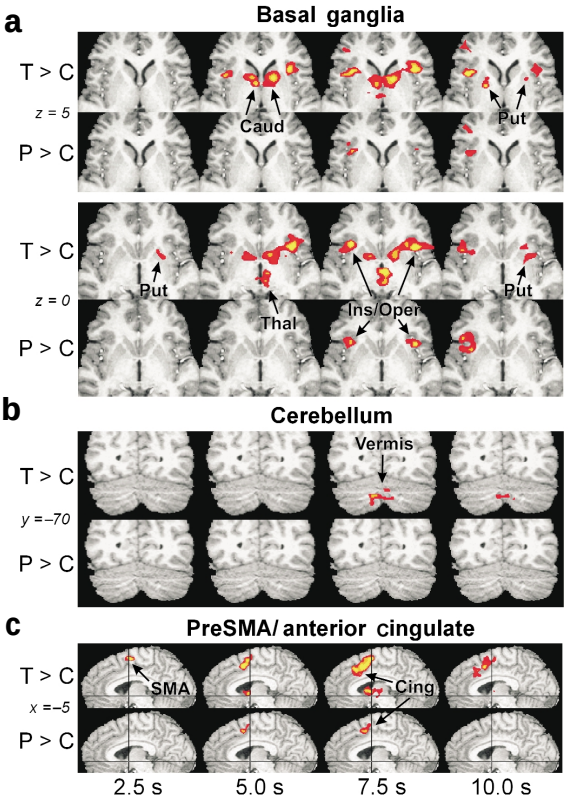

Fig. 4. Activation foci in the basal ganglia (**a**), cerebellum (**b**), and pre-supplementary motor area/anterior cingulate (**c**) resulting from subtraction of the control (C) condition from the time (T) and the pitch (P) perception conditions at 2.5, 5.0, 7.5 and 10.0 s after trial onset. Significant foci ($p < 0.001$) are displayed with a red-yellow intensity scale denoting greater activation for the T or P conditions. Slices are displayed in neurological view (left is on the viewer's left). Location of slices defined by the distance (mm) from anterior commissure: *x*, right (+)/left (–); *y*, anterior (+)/posterior (–); *z*, superior (+)/inferior (–). Caud, caudate nucleus; Cing, anterior cingulate area; Ins, insula; Oper, frontal operculum; Put, putamen; Thal, thalamus; SMA, supplementary motor area.

T and P conditions (Table 2), and included the inferior frontal gyrus (Broca's area, BA 44/45), intraparietal sulcus (BA 40), superior parietal lobule/precuneus (BA 7) and DLPF cortex.

The results from the T minus P subtraction were similar to the results for the T minus C subtraction (Fig. 6). During the earlier imaging epochs (2.5 and 5.0 s), subcortical activations unique to the T condition were in the right hemisphere and included the putamen (*x*, *y*, *z* = 24, 7, –2), caudate (15, 6, 13) and insula/frontal operculum (29, 16, 2). The later region, however, was also activated during the 7.5-s epoch in the pitch condition (Table 2, Fig. 4a). During the later imaging epochs (7.5 s), the right DLPF cortex (21, 21, 30) was also unique to the T condition (Fig. 6).

Discussion

The present findings provide compelling evidence for the involvement of the basal ganglia in formulating representations of time. Activation in the right putamen and caudate were uniquely associated with encoding time intervals. These results corroborate studies in Parkinson's disease showing that dopaminergic treatment improves motor timing[30,31] and time perception[32]. Pharmacological challenges in animals also suggest that dopaminergic antagonists and agonists respectively slow down and speed up timing operations[12,13]. Contrary to one proposal[33], these and other studies[10,11,27] show that the basal ganglia are involved in timing a wide range of intervals, from hundreds of milliseconds (300 ms) to tens of seconds (20 s). Collectively, these results implicate striatal dopaminergic neurotransmission in hypothetical internal timekeeping mechanisms.

Table 2. Stereotaxic brain atlas coordinates[49] for regions commonly activated in subtractions of Time and Pitch perception conditions relative to Control condition.

		Time > Control				Pitch > Control			
Location (Brodmann Area)	**Hemisphere**	**2.5**	**5.0**	**7.5**	**10.0**	**2.5**	**5.0**	**7.5**	**10.0**
Frontal									
Insula/operculum (47)	R		31, 17, 3	35, 16, 3	34, 17, 4			34, 17, 0	
	L		–35, 11, 5	–34, 15, 2	–36, 12, 4			–34, 18, 1	–36, 17, 0
PreSMA (6),									
Anterior cingulate (32)	L	–4, –1, 56	–4, 6, 49	–7, 10, 45	–5, 12, 43		–6, 7, 48	–4, 8, 49	
Inferior frontal gyrus (44/45)	R			37, 1, 32				37, 4, 28	
	L			–46, 4, 21	–47, 5, 18			–45, 4, 22	–44, 7, 26
Dorsolateral (46/10/9)	L			–39, 42, 12	–36, 46, 13				–36, 40, 8
				–42, 26, 28	–40, 14, 29				
Parietal									
Intraparietal sulcus,									
Angular gyrus (40)	L			–31, –49, 37	–29, –52, 33				
				–36, –53, 44			–32, –47, 38	–30, –55, 36	
Superior parietal lobule,									
Precuneus (7)	L			–21, –66, 49	–28, –49, 43			–13, –72, 50	–43, –57, 50
					–21, –63, 51				–25, –65, 50

R, right; L, left; B, bilateral

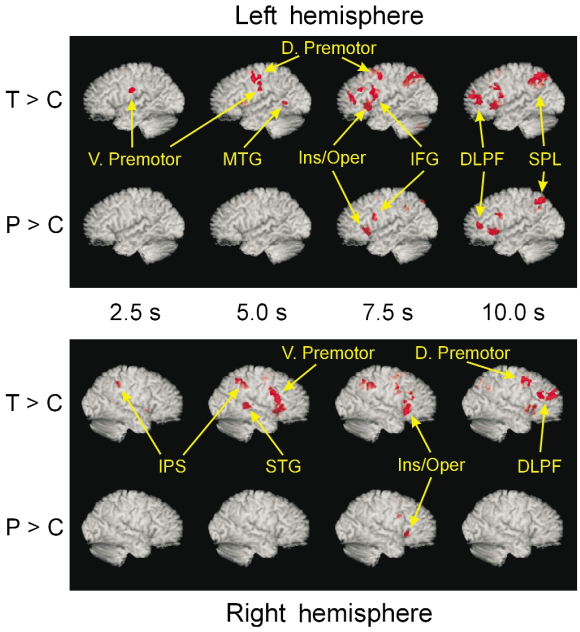

Fig. 5. Activation foci in the lateral surface of the left and right hemispheres denote greater activation for the time (T) and the pitch (P) perception conditions relative to the control (C) condition at 2.5, 5.0, 7.5 and 10.0 s after trial onset. Significant foci ($p < 0.001$) are displayed in red. DLPF, dorsal lateral prefrontal cortex; D. Premotor, dorsal premotor; IFG, inferior frontal gyrus; Ins, insula; IPS, inferior parietal sulcus; MTG, middle temporal gyrus; Oper, frontal operculum; STG, superior temporal gyrus; V. Premotor, ventral premotor.

Our findings did not support a unique role for the cerebellum in encoding time intervals. Nonetheless, cerebellar activation was observed during the time perception task (T minus C), consistent with several studies showing diminished time perception in patients with cerebellar damage[16,18,34]. However, in our study, activation was in the vermis rather than the lateral cerebellar hemispheres, contrary to reports that damage to the lateral cerebellum, but not the vermis, correlated with time perception deficits[15,18]. Cerebellar activation evolved later in the course of the trial, just before and during movement execution, suggesting an involvement in processes other than explicit timing. This is consistent with our previous fMRI study[27] showing that cerebellar activation was not specific to timing self-paced finger movements. Apart from its well-documented role in sensorimotor processing, neuroimaging research indicates that the cerebellum participates in many cognitive functions, including tactile perception[35] and working memory[36]. One lesion study has also shown that cerebellar damage produces pitch perception deficits[14]. Its broad role in sensorimotor and cognitive processing[37] has suggested that the cerebellum monitors and adjusts input from the cerebral cortex, but is not involved in computing a specific operation *per se*[38]. By this account, later activation in vermal lobule VIIB, which receives auditory and visual input[39], could be due to its involvement in optimizing sensory input from auditory systems, which facilitates the comparison of intervals in working memory. Although other explanations are possible, this account is appealing because it predicts that damage to the cerebellum will slow sensory acquisition, which should disrupt a broad range of behaviors, especially those involving timing. This view may explain why patients with cerebellar damage show deficits in timing[16,17], but not always in the perception of pitch or loudness[16,18].

Representations of time depend on the interplay of internal timekeepers with attention and working memory, functions more commonly identified with cortical systems. Neural systems associated with these functions should support a variety of computations, which may explain why they were not always unique to timing intervals (T minus P). However, in the comparisons involving the control condition (T minus C, P minus C), right hemisphere activations were observed during time but not pitch perception. These later results are consistent with findings from converging neuroscience approaches. Specifically, a neuroanatomical bridge for basal ganglia–cortical interactions is the thalamus[40], which was activated early during the encoding of intervals, along with two cortical regions, suggesting they work together in formulating representations of time. Coupled activation in the right inferior parietal cortex may suggest an interdependent role of this region in attention, which theoretically regulates the timekeeping mechanism. Neurological patients with right but not left inferior parietal damage show time, but not pitch, perception deficits that correlate with impairments in switching attention[21]. Electrophysiological recordings in humans have also shown a right hemisphere bias for temporal processing[41], especially in the parietal cortex[42]. The close relationship between timekeeping and attention is presumed by one influential theory[2], and has received empirical support in behavioral studies conducted on humans[4,5]. According to this view, representations of time are reflected in the pulse count accumulated over

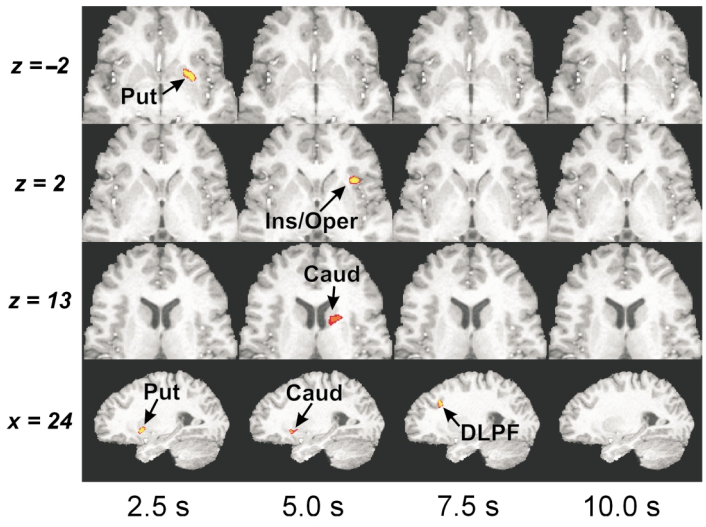

Fig. 6. Activation foci in the basal ganglia, insula/frontal operculum and dorsal lateral prefrontal cortex resulting from greater activation for the time (T) relative to the pitch (P) perception conditions at 2.5, 5.0, 7.5 and 10.0 s after trial onset. Significant foci ($p < 0.001$) are displayed with a red-yellow intensity scale. Slices are displayed in neurological view (left is on the viewer's left). Location of slices defined by the distance (mm) from anterior commissure. Caud, caudate nucleus; DLPF, dorsal lateral prefrontal cortex; Ins, insula; Oper, frontal operculum; Put, putamen.

a particular physical time, which critically depends on the degree of attentional engagement. Our results point to the right inferior parietal cortex in regulating the accumulation of pulses, because of its well-documented involvement in attention[43]. Bilateral projections from the inferior parietal cortex to the putamen and caudate nucleus in monkeys[44] provide a neuroanatomic basis for the interaction of attention and timekeeping operations.

The perception of time also relies on stored representations of intervals in working memory[2]. During time perception, activation was observed in regions commonly associated with temporary storage functions, including the bilateral premotor (BA 6) and right DLPF cortex (BA 9, 10, 46)[19,20,45]. Right DLPF activation was also unique to performing time discriminations. This corroborates our previous finding that damage to these same regions in the right, but not left, hemisphere produces time perception deficits[21]. Controversy exists over whether these areas support different working memory functions[45–47]. However, a recent meta-analysis of neuroimaging studies[20] implicated the premotor cortex in a 'rehearsal circuit' in tasks involving mainly the temporary maintenance of information, such as item recognition. In contrast, the DLPF cortex was associated with an 'executive circuit' in tasks requiring manipulation of stored information, such as the two- and three-back working-memory tasks. Our findings are compatible with this process distinction, as premotor cortex activation began early, consistent with the need for maintaining the standard interval during the trial, whereas DLPF cortex activation unfolded later in association with comparing the two intervals and selecting a response. Independent evidence for the DLPF cortex in executive functions of working memory was observed in the pitch condition as well, in which activation unfolded later during the comparison phase, but was confined to the left hemisphere. Though premotor cortex was not activated in the pitch condition, repeated presentation of the standard pitch across the trial may have minimized the need for rehearsal.

In summary, the present results are compatible with prevailing cognitive theory, and provide new insights into the evolution of activation in cortical and subcortical systems that are specific to different cognitive components of a time perception task. The reciprocal interactions among these specialized systems give rise to our perception of current time. The results are in agreement with converging avenues of research implicating a perceptual system in which the basal ganglia act as a timekeeper that is tightly coupled with an attention system in the right inferior parietal cortex. This right hemisphere bias for the encoding of temporal information is in agreement with converging focal lesion and electrophysiological research in humans. The distinct evolution of activation in the bilateral premotor and right DLPF systems, together with previous neuroimaging studies, provides evidence for different working memory functions underlying time perception. Our results also showed that time and pitch discriminations are mediated by shared parietal and prefrontal systems mostly in the left hemisphere, which were activated during decision and response selection components of both tasks. Presently, we are investigating the dynamics of brain activation patterns during longer delay periods to more directly distinguish systems involved in encoding and short-term maintenance of time intervals.

METHODS

Subjects. Right-handed subjects (2 male/15 female; mean age, 23.9 years) gave written informed consent and were compensated for participation. The experimental protocol was approved by the institutional review board of the Medical College of Wisconsin.

Experimental design. Tone stimuli were presented binaurally using a computer playback system. Sounds were amplified near the scanner and delivered to the subject via air conduction through 180-cm paired plastic tubes, which were threaded through tightly occlusive ear inserts that attenuated background scanner noise to approximately 75 dB sound pressure level (SPL). Background scanner noise consisted of pulses occurring every 205 ms throughout the imaging run; the intensity of the tone stimuli averaged 100 dB SPL. For all three conditions, the standard tones were 700 Hz in pitch separated by a 1200 ms interval (Fig. 1). In the T condition, the eight comparison intervals were ±60-ms increments of the standard interval, and were presented twice in a randomized order (16 trials); pitch did not vary across the four tones. In the P condition, the eight comparison tone pitches were ±4 Hz increments of the standard 700 Hz tones and were presented twice in a randomized order (16 trials); duration did not vary during this condition. In the C task, 16 trials of identical standard tones were presented. The C task was a baseline condition used for removing the effects of low-level sensory and motor processing from the functional maps in the two discrimination conditions. Subjects pressed one of two keys with their right index or middle finger to indicate longer/higher or shorter/lower in the discrimination conditions; subjects pressed a key using their index in the control task. Accuracy and reaction time were measured with a nonferrous key-press pad. Subjects briefly practiced the three conditions before scanning.

Image acquisition. Event-related fMRI was done on a 1.5T GE Signa (Waukesha, Wisconsin) scanner equipped with a three-axis local gradient head coil and an elliptical endcapped quadrature radiofrequency coil. Foam padding limited head motion within the coil. Echo-planar images were collected using a single-shot, blipped gradient-echo echo-planar pulse sequence (TE, 40 ms; TR, 2.5 s; 90° flip angle; FOV, 240 mm; resolution, 64 × 64 matrix). Seventeen contiguous sagittal 7-mm-thick slices were acquired to provide coverage of the entire brain. Scanning was synchronized with the onset of the first tone so that 7 images were acquired during each 17.5-s trial (Fig. 2) with a total of 112 images per run (16 trials per run). An additional 4 images (10.0 s) were added to the beginning of the run to allow the MR signal to reach equilibrium, and were discarded from further analysis; 4 images were added to the end of the run to accommodate the delayed rise of the hemodynamic response. Before functional imaging, high-resolution three-dimensional spoiled gradient-recalled at steady-state anatomic images were collected (TE, 5 ms; TR, 24 ms; 40° flip angle; NEX, 1; slice thickness, 1.2 mm; FOV, 24 cm; resolution, 256 × 128) for anatomic localization and co-registration.

fMRI data analysis. Functional images were generated using Analysis of Functional NeuroImages[48] software. Time series images were spatially registered in three-dimensional space to minimize effects of head motion. A deconvolution analysis was used to generate impulse response functions (IRFs) of the fMRI signal on a voxel-wise basis. This analysis produced an estimate of the hemodynamic response for each condition (T, P and C) relative to a baseline state (rest) without making *a priori* assumptions regarding the shape, delay or magnitude of the IRF. Anatomical and functional images were then interpolated to volumes with 1 mm^3 voxels, co-registered, converted to Talairach stereotaxic coordinate space[49], and blurred using a 4 mm Gaussian full-width half-maximum filter. Voxel-wise analyses of variance (T versus C, P versus C, and T versus P conditions) were done separately for images obtained at 2.5, 5.0, 7.5 and 10.0 s after trial onset. Pooled-variance *t*-tests were applied on a voxel-wise basis to the IRF estimates for each epoch to identify regions showing greater activation in the T and P discrimination conditions relative to the C condition and greater activation in the T than the P condition. An activated region was defined by an individual voxel probability less than 0.001 ($t > 3.61$; df, 16), and a minimum cluster size threshold of 300 microliters[50]. These two thresholds were established based on 10,000 Monte Carlo simulations demonstrating that the chance probability of obtaining a significant activation cluster for an entire volume (type I error) was less than 10^{-6}.

ACKNOWLEDGEMENTS

This study was funded in part by grants from the Department of Veterans Affairs and National Foundation for Functional Brain Imaging (D.L.H.), the National Institutes of Health (P01 MH51358, R01 MH57836, M01 RR00058) and W.M. Keck Foundation (S.M.R.). We thank R. Cox, E. DeYoe, S. Durgerian, R. Lee, G. Mallory, L. Mead, J. Neitz and B. Ward for their assistance.

RECEIVED 6 SEPTEMBER; ACCEPTED 21 DECEMBER 2000

1. Wearden, J. H. "Beyond the fields we know...": Exploring and developing scalar timing theory. *Behavioural Processes* 45, 3–21 (1999).
2. Gibbon, J., Church, R. M. & Meck, W. H. Scalar timing in memory. *Ann. NY Acad. Sci.* 423, 52–77 (1984).
3. Matell, M. S. & Meck, W. H. Neuropsychological mechanisms of interval timing behavior. *Bioessays* 22, 94–103 (2000).
4. Brown, S. W. Time perception and attention: the effects of prospective versus retrospective paradigms and task demands on perceived duration. *Percept. Psychophys.* 38, 115–124 (1985).
5. Zakay, D. & Block, R. A. in *Time, Internal Clocks, and Movement* (eds. Pastor, M. A. & Artieda, J.) 143–164 (Elsevier Science BV, Amsterdam, 1996).
6. Baddeley, A. *Working Memory* (Clarendon/Oxford Univ. Press, Oxford, 1986).
7. Harrington, D. L. & Haaland, K. Y. Neural underpinnings of temporal processing: A review of focal lesion, pharmacological, and functional imaging research. *Rev. Neurosci.* 10, 91–116 (1999).
8. Narabayashi, H. & Nakamura, R. in *Clinical Neurophysiology of Parkinsonism*. (eds. Delwaide, P. J. & Agnoli, A.) 45–57 (Elsevier, New York, 1985).
9. Manto, M. Pathophysiology of cerebellar dysmetria: the imbalance between the agonist and the antagonist electromyographic activities. *Eur. Neurol.* 36, 333–337 (1996).
10. Artieda, J., Pastor, M. A., Lacruz, F. & Obeso, J. A. Temporal discrimination is abnormal in Parkinson's disease. *Brain* 115, 199–210 (1992).
11. Harrington, D. L., Haaland, K. Y. & Hermanowicz, N. Temporal processing in the basal ganglia. *Neuropsycholologia* 12, 3–12 (1998).
12. Maricq, A. V. & Church, R. M. The differential effects of haloperidol and methamphetamine on time estimation in the rat. *Psychopharmacology* 79, 10–15 (1983).
13. Meck, W. H. Affinity for the dopamine D2 receptor predicts neuroleptic potency in decreasing the speed of an internal clock. *Pharmacol. Biochem. Behav.* 25, 1185–1189 (1986).
14. Casini, L. & Ivry, R. Effects of divided attention on temporal processing in patients with lesions of the cerebellum or frontal lobe. *Neuropsychologia* 13, 10–21 (1999).
15. Ivry, R. B., Keele, S. W. & Diener, H. C. Dissociation of the lateral and medial cerebellum in movement timing and movement execution. *Exp. Brain Res.* 73, 167–180 (1988).
16. Ivry, R. B. & Keele, S. W. Timing functions of the cerebellum. *J. Cogn. Neurosci.* 1, 136–152 (1989).
17. Malapani, C., Dubois, B., Rancurel, G. & Gibbon, J. Cerebellar dysfunctions of temporal processing in the seconds range in humans. *Neuroreport* 9, 3907–3912 (1998).
18. Mangels, J. A., Ivry, R. & Shimizu, N. Dissociable contributions of the prefrontal and neocerebellar cortex to time perception. *Cogn. Brain Res.* 7, 15–39 (1998).
19. Goldman-Rakic, P. S. Regional and cellular fractionation of working memory. *Proc. Natl. Acad. Sci. USA* 93, 13473–13480 (1996).
20. Smith, E. & Jonides, J. Storage and executive processes in the frontal lobes. *Science* 283, 1657–1661 (1999).
21. Harrington, D. L., Haaland, K. Y. & Knight, R. T. Cortical networks underlying mechanisms of time perception. *J. Neurosci.* 18, 1085–1095 (1998).
22. Meck, W. H., Church, R. M., Wenk, G. L. & Olton, D. S. Nucleus basalis magnocellularis and medial septal area lesions differentially impair temporal memory. *J. Neurosci.* 7, 3505–3511 (1987).
23. Halsband, U., Ito, N., Tanji, J. & Freund, H. J. The role of premotor cortex and the supplementary motor area in the temporal control of movement in man. *Brain* 116, 243–266 (1993).
24. Larsson, J., Gulyas, B. & Roland, P. E. Cortical representation of self-paced finger movement. *Neuroreport* 7, 463–468 (1996).
25. Lejeune, H. *et al.* The basic pattern of activation in motor and sensory temporal tasks: positron emission tomography data. *Neurosci. Lett.* 235, 21–24 (1997).
26. Penhune, V. B., Zatorre, R. J. & Evans, A. Cerebellar contributions to motor timing: a PET study of auditory and visual rhythm reproduction. *J. Cogn. Neurosci.* 10, 752–765 (1998).
27. Rao, S. M. *et al.* Distributed neural systems underlying the timing of movements. *J. Neurosci.* 17, 5528–5535 (1997).
28. Jueptner, I. H. *et al.* Localization of a cerebellar timing process using PET. *Neurology* 45, 1540–1545 (1995).
29. Maquet, P. *et al.* Brain activation induced by estimation of duration: a PET study. *Neuroimage* 3, 119–126 (1996).
30. O'Boyle, D. J., Freeman, J. S. & Cody, F. W. J. The accuracy and precision of timing of self-paced, repetitive movements in subjects with Parkinson's disease. *Brain* 119, 51–70 (1996).
31. Pastor, M. A., Artieda, J., Jahanshahi, M. & Obeso, J. A. Performance of repetitive wrist movements in Parkinson's disease. *Brain* 115, 875–891 (1992).
32. Malapani, C. *et al.* Coupled temporal memories in Parkinson's disease: a dopamine-related dysfunction. *J. Cogn. Neurosci.* 10, 316–331 (1998).
33. Ivry, R. The representation of temporal information in perception and motor control. *Curr. Opin. Neurobiol.* 6, 851–857 (1996).
34. Casini, L. & Macar, F. Effects of attention manipulation on judgments of duration and of intensity in the visual modality. *Mem. Cognit.* 25, 812–818 (1997).
35. Gao, J. H. *et al.* Cerebellum implicated in sensory acquisition and discrimination rather than motor control. *Science* 272, 545–547 (1996).
36. Desmond, J. E., Gabrieli, J. D. E., Wagner, A. D., Ginier, B. L. & Glover, G. H. Lobular patterns of cerebellar activation in verbal working-memory and finger-tapping tasks as revealed by functional MRI. *J. Neurosci.* 17, 9675–9685 (1997).
37. Schmahmann, J. D. *The Cerebellum and Cognition* (Academic, New York, 1997).
38. Bower, J. M. Is the cerebellum sensory for motor's sake, or motor for sensory's sake: the view from the whiskers of a rat? *Prog. Brain Res.* 114, 463–496 (1997).
39. Brodal, P. The ponto-cerebellar projection in the rhesus monkey: an experimental study with retrograde axonal transport of horseradish peroxidase. *Neuroscience* 4, 193–208 (1979).
40. Alexander, G. E., DeLong, M. R. & Strick, P. L. in *Annual Review of Neuroscience* (ed. Cowan, W. M.) 357–381 (Society for Neuroscience, Washington, DC, 1986).
41. Brunia, C. & Damen, E. Distribution of slow brain potentials related to motor preparation and stimulus anticipation in a time estimation task. *Electroencephalogr. Clin. Neurophysiol.* 69, 234–243 (1988).
42. Mohl, W. & Pfurtscheller, G. The role of the right parietal region in a movement time estimation task. *Neuroreport* 2, 309–312 (1991).
43. Posner, M. I., Walker, J. A., Friedrich, F. J. & Rafal, R. D. Effects of parietal injury on covert orienting of attention. *J. Neurosci.* 4, 1863–1874 (1984).
44. Cavada, C. & Goldman-Rakic, P. S. Topographic segregation of corticostriatal projections from posterior parietal subdivisions in the macaque monkey. *Neuroscience* 42, 683–696 (1991).
45. Cohen, J. *et al.* Temporal dynamics of brain activation during a working memory task. *Nature* 386, 604–607 (1997).
46. Awh, E., Smith, E. E. & Jonides, J. Human rehearsal processes and the frontal lobes: PET evidence. *Ann. NY Acad. Sci.* 769, 97–117 (1995).
47. Prabhakaran, V., Narayanan, K., Zhao, Z. & Gabrieli, J. D. E. Integration of diverse information in working memory within the frontal lobe. *Nat. Neurosci.* 3, 85–90 (2000).
48. Cox, R. W. AFNI: Software for analysis and visualization of functional magnetic resonance neuroimages. *Comput. Biomed. Res.* 29, 162–173 (1996).
49. Talairach, J. & Tournoux, P. *Co-Planar Stereotaxic Atlas of the Human Brain* (Thieme, New York, 1988).
50. Forman, S. D. *et al.* Improved assessment of significant activation in functional magnetic resonance imaging (fMRI): use of a cluster-size threshold. *Magn. Reson. Med.* 33, 636–647 (1995)